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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/993,287	11/23/2001	George Jackowski	2132.108	5379

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EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 01/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/993,287	JACKOWSKI ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 39-46* is/are pending in the application.

4a) Of the above claim(s) *39-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1 and 39-46* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/12/02 & 9/29/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicants amendment filed December 10, 2004 is acknowledged. Claim 1 has been modified. Claims 2-38 were canceled without prejudice or disclaimer. New claims 39-46 have been added. Currently claims 1 and 39-46 are pending and under consideration. The new claims have been considered and are restricted below.

Election/Restrictions

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claim 1 is drawn to a biopolymer consisting of SEQ ID NO:1 classified in class 530, subclass 300 or class 530, subclass 350 for example.

II. Claims 39-43 are drawn to methods comparing peptide profile of patient samples to SEQ ID NO:1 classified in class 436, subclass 518 and class 424, subclass 93.1 for example.

III. Claims 44-46 are drawn to kits containing the peptide consisting of SEQ ID NO:1 and antibodies to bind the peptide, classified in class 422, subclass 61 for example.

3. The inventions are distinct, each from the other because of the following reasons:

A. Inventions **I** and **II** are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the peptide product (SEQ ID NO:1) of invention I can be used in other materially different processes. The peptide of inventive group I is not limited to the mass spectrometric protein profiling procedure of invention II but can be utilized to make antibodies or in antibody binding processes for identification and/or purification.

B. Inventions **I and III** are drawn to two disclosed patentably distinct inventions (a biopolymer and a kit). Group I is directed to a biopolymer while Group III is directed to kits comprising the peptide consisting of SEQ ID NO:1 and antibodies that bind SEQ ID NO:1. The two products are independent and require different searches. The kit of Group III contains antibodies and therefore required a separate search. These separate products/compositions bear distinct structural or biochemical properties Therefore, each disclosed patentably distinct composition is considered a separate invention. In other words, the biopolymer (polypeptides) and kits contained biopolymer (polypeptides) and antibodies are patentably distinct in terms of structure and function (antibody vs. peptide).

C. The method and kit inventions of Group **II** and Group **III** are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the inventive method and kit are patentably distinct. The method of Group II *merely detects* SEQ ID NO:1 while Group III is drawn to kits comprising SEQ ID NO:1 and antibodies to the peptide. The method of Group II does not require antibodies. Accordingly, restriction is proper.

It is recognized that although the search for the inventions may overlap they are not totally co-extensive, where the search for one would fully encompass the search for the others. Because these inventions are distinct for the reasons given above and the search required for Inventions I-III are not mutually inclusive (i.e. the search for one invention is not required for the other inventions) restriction for examination purposes as indicated is proper.

4. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper. Please note that the classifications in the restriction are illustrative only and **do not** represent all the classes and subclasses which must be searched for each invention; nor is the search limited to issued US patents, but rather includes foreign patents and applications as well as literature searches.

5. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

6. Applicant's election with traverse of Group I (claim 1) in the reply filed on 12/10/04 is acknowledged. Applicant's traversal is on the ground(s) that amino acid sequences numbered one through three are related as a Markush-type grouping because they share a common utility (all related to Type II diabetes) and share a common structural feature (all fragments of the same parent protein –complement C3 precursor protein). This traversal was carefully considered and found persuasive. The restriction between sequence identification numbers 1, 2, and 3 of record in the paper mailed 10/6/04 is vacated.

7. The requirement set forth above is deemed proper and is therefore made FINAL.

8. Claims 39-46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10 December 2004.

9. Currently claim 1 is under consideration.

Priority

10. The instant application does not claim priority or benefits to an earlier application.

Information Disclosure Statement

11. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the Examiner on form PTO-892 or Applicant on form PTO-1449 has cited the references they have not been considered.

12. The information disclosure statements filed 3/12/02 and 9/29/03 have been considered as to the merits prior to first action.

Oath/Declaration

13. A new oath or declaration is required because the date for Dr. John Marshall (inventor 2) is omitted. The wording of an oath or declaration cannot be amended. If the wording is not correct or if all of the required affirmations have not been made or if it has not been properly subscribed to, a new oath or declaration is required. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02.

Specification

14. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

I. The use of the trademarks has been noted in this application. (.i.e. SEPHAROSE on page 41 lines 4 and 5, TRITON on page 42 line 12). They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Abstract

15. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited.

The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

16. The instant application includes legal phraseology "said". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

17. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 1 is vague and indefinite because the biopolymer is "diagnostic" for Type II diabetes. "Diagnostic" reads on not only the detection of the disease but also the analysis of the cause or nature of the disease. It is not clear how the biopolymer marker will analyze the cause or nature of Type II diabetes. Applicants intended meaning of "diagnostic" is not defined by the claims or the specification. The specification does not provide a standard for ascertaining the requisite degree and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is suggested that the claim merely recite "detection of" Type II diabetes in order to obviate this rejection.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

18. Claim 1 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial, credible or asserted utility or a well-established utility.

Claim 1 is drawn to a biopolymer marker consisting of SEQ ID NO:1 having utility as a diagnostic marker for Type II diabetes. The biopolymer marker is recited to be useful in methods determining the absence or presence as well as differential regulation of SEQ ID NO:1, wherein the absence of SEQ ID NO:1 indicates that the subject has Type II diabetes.

These diagnostic methods include for example biopolymer evidencing, characterization, regulation, risk-assessment, and therapeutic identification. The specification also contemplates the use of these methods for diagnosing, staging, monitoring, prognosticating or determining predisposition to Type II diabetes.

Applicants have disclosed in the specification that SEQ ID NO: 1 is measurable in normal patients but non detectable in Type II diabetes. See page 46 lines 8-18. However, this disclosure appears to require not only SEQ ID NO:1 but a combination of SEQ ID Nos: 1-3 for the identification of Type II diabetes.

Applicant also sets forth figure 1 as evidence of SEQ ID NO:1 as a marker for Type II diabetes. However, figure 1 appears to show SEQ ID NO:1 in normal patients as well as Type II diabetes patients. No clear difference in up and down regulation of the marker can be determined. Therefore, SEQ ID NO:1 does not appear to be a marker for Type II diabetes (clearly distinguishing the disease from control or normal patients. See Band 3-2 in figure 1. There are no disclosure or working examples that demonstrate the specifically asserted utility and evidences a substantial utility was well established at the time of filing. The specification does not enable one of ordinary skill in the art to definitively assess the incidence of the disease in a single test sample. Furthermore, Applicants have not provided any disclosure enabling the use of the biopolymer marker with regard to regulating the presence or absence of said sequence. The disclosure is equally lacking any teaching for how the identified sequence will be utilized to identify therapeutic avenues and regulate a disease state. Accordingly, the specification does not identify a specific, substantial, credible or asserted utility or a well-established utility for SEQ ID NO:1.

There is no disclosure designating how the sequence bound in these methods could be regarded as enabling one of ordinary skill in the art to use SEQ ID NO:1 as a diagnostic marker.

Applicants have not set forth any supporting evidence that suggests that SEQ ID NO: 1 is a unique molecular markers for type II diabetes. Based on the analysis set forth above the specification does not exemplify sufficient findings that constitute a specific, substantial or credible utility.

Claim 1 is also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by a specific, substantial or credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

19. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

Claim 1 is directed to a biopolymers consisting of SEQ ID NO:1 diagnostic for Type II diabetes. However, the specification does not support this assertion. The specification (in particular page 46) and figure 1 do not definitively correlate the absence of the claimed marker consisting of SEQ ID NO:1 to Type II diabetes.

Specifically, the specification recites that the biopolymer consisting of SEQ ID NO:1 is found in the serum of normal patients but not in patients suffering from Type II diabetes on page 46 but does not contain any data supporting this contention and the figures exemplify SEQ ID NO:1 in both normal and Type II diabetes patients (See figure 1 Band 3-2). Therefore it is unclear how SEQ ID NO:1 is identified as a "notable sequence" or how they were deemed "evidentiary" of a disease state (Type II diabetes). There is nothing in the disclosure that would enable one to choose SEQ ID NO:1 as notable sequences among an infinite number of possible proteins or peptides present in a patient sample. There is no correlation between the procedure for screening samples from patients suspected of having a variety of different disease, the presence/absence of SEQ ID NO:1, and the determination, prediction, assessment of Type II diabetes.

Furthermore, Applicants have not provided any disclosure enabling the use of the biopolymer marker with regard to regulating the presence or absence of said sequence. The disclosure is equally lacking any teaching for how the identified sequence will be utilized to identify therapeutic avenues and regulate a disease state. There is no disclosure designating how the sequence could be utilized therein, enabling one of ordinary skill in the art to use the sequences in the diagnostic method.

Applicants have not set forth any supporting evidence that suggests that SEQ ID NO:1 is a unique molecular marker for Type II diabetes or any other disease and the prior art teaches that disease markers are highly unpredictable and require extensive experimentation.

Tascilar et al. (Annals of Oncology 10,Suppl. 4:S107-S110, 1999) reports on diagnostic methods in the realm of disease states, however this review article is relevant to Applicants' claimed invention. It is art known that molecular–based assays are valid tools used in predicting and detecting diseases, however as assessed in the Tascilar review "...these tests should be interpreted with caution...". and "the genetic changes found in sources other than the pancreas itself (blood, stool) should be evaluated prudently".

Furthermore, Tockman et al. (Cancer Research 52:2711s-2718s, 1992) teach considerations necessary for a suspected cancer biomarker (intermediate end point marker) to have efficacy and success in a clinical application. Although the reference is drawn to biomarkers for early lung cancer detection, the basic principles taught are clearly applicable to other oncogenic disorders.

Tockman teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials, see abstract. Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and **if validated** (emphasis added) can be used for population screening (p. 2713s, column 1).

The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and *link* those marker results with subsequent histological confirmation of disease.

"This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point [marker]", see page 2714s, column 1, Biomarker Validation against Acknowledged Disease End Points section. Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials, see page 2716s, column 2, Summary section. Tockman reiterates that the predictability of the art in regards to cancer prognosis and the estimation of life expectancies within a population with a disease or disorder are highly speculative and unpredictable.

The instant disclosure has not addressed the issues taught in the prior art as crucial to the discovery of a biopolymer marker.

The nature of the invention- the invention is directed to disease markers or biopolymers.

The state of the prior art- the prior art of record fails to disclose the particular biopolymers in any disease state.

The predictability or lack thereof in the art- there is no predictability based on the instant specification that the biopolymers are indicative of any disease state including Type II diabetes.

The amount of direction or guidance present- appropriate guidance is not provided by the specification for the claimed biopolymers.

The presence or absence of working examples- working examples are not provided in the specification that exemplify the biopolymers as markers for any disease.

The quantity of experimentation necessary- it would require undue amount of experimentation for the skilled artisan to make and use the biopolymers as claimed.

*The relative skill of those in the art-*the level of skill in the art is high.

The breadth of the claims- as recited, the instant claims are directed to a biopolymer consisting of SEQ ID NO:1 being a diagnostic for Type II diabetes.

While it is not necessary to show working examples for every possible embodiment, there should be sufficient teachings in the specification that would suggest to the skilled artisan that the breadth of the claimed biopolymer is enabled. This is not the case in the instant specification.

In view of the teachings of In re Wands, 8 USPQ2d 1400, it has been determined that the level of experimentation required to enable the breadth of the claims is undue.

Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966).

While every aspect of a generic claim does not have to be carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. Genetech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001. That requirement has not been met in this specification with respect to the biopolymer consisting of SEQ ID NO:1 diagnostic for Type II diabetes.

Therefore, in view of the insufficient guidance in the specification, extensive experimentation would be required to enable the claims and to practice the invention as claimed.

20. For reasons aforementioned, no claims are allowed.

21. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to Group TC 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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